3-Amino-*o*-Phthalic Acid and Certain of Its Derivatives.

A DISSERTATION

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY.

BY

FAREL LOUIS JOUARD

NEW YORK CITY

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EASTON, PA.:
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To My Father and Mother

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The work described in the following pages was undertaken at the suggestion of Professor Marston T. Bogert, and was carried out under his direction.

The author wishes to thank him for the kindly interest shown and for the many helpful suggestions offered during the progress of these investigations. F. L. J.

3-Amino-*o*-Phthalic Acid and Certain of Its Derivatives.

Historical Part.

Although numerous references to 3-aminophthalic acid are found in the literature, the properties ascribed to this compound by previous investigators are singularly contradictory and confusing. In fact, in view of the results described in the latter part of this work, it is rather doubtful if the acid has ever before been prepared in the pure state. The present work, therefore, besides being a continuation of the researches on the nitrophthalic acids[11] and on 4-aminophthalic acid[18,19] recently carried on in this laboratory, was undertaken in order to isolate 3-aminophthalic acid definitely, to investigate its properties, and to make a systematic study of its simple derivatives, very few of which were known.

The first mention of "aminophthalic acid" was made in 1863, by Miller,[1] who obtained a lemon-yellow crystalline product by the reduction of "nitrophthalic acid." This investigator observed the strong uranium-like fluorescence of solutions of the compound, but does not describe his method of reduction nor give any tangible data.

In 1871, Faust[2] reduced "nitrophthalic acid" with tin and hydrochloric acid, and found that *m*-aminobenzoic acid was thus formed. It is to be remembered that at that time the two isomeric nitrophthalic acids produced by the nitration of phthalic acid had not yet been differentiated, and that Miller and Faust were therefore experimenting upon mixtures of the two.

It was not until seven years later that Miller[4,5] discovered the isomerism of the two nitro acids and succeeded in separating them. In 1881 he furthermore reduced each of the isomers with tin and hydrochloric acid,[6] and in the case of 3-nitrophthalic acid obtained a product which he considered the tin double salt of 3-aminophthalic acid. In attempting to de-tin this salt with hydrogen sulphide, he found that a loss of carbon dioxide occurred, leaving *m*-aminobenzoic acid.

In 1901, Onnertz[12] again carried out Miller's reduction of 3-nitrophthalic acid, using precautions, however, against an elimination of carbonic anhydride. To this end, he evaporated the de-tinned product to dryness at a lower temperature, under diminished pressure, and finally obtained a yellow crystalline product darkening at 174° and melting at 184–6°, with evolution of carbon dioxide. This substance he supposed to be 3-aminophthalic acid, but the analytical data given are not very convincing. By using ferrous hydroxide instead of tin and hydrochloric acid as a reducing agent, Onnertz also obtained a white crystalline substance, the melting-point of which he does not mention, but whose silver salt showed a silver content closely agreeing with that of an aminophthalate.

During the same year, Seidel[13] reduced 3-nitrophthalic acid with sodium sulphide, thereby obtaining a soft yellow powder melting at 226° and soluble in water and in alcohol with greenish fluorescence. His analytical figures correspond fairly well with those of 3-aminophthalic acid, but the details of the reduction are not given.

In 1903, Kauffmann and Beisswenger[15] repeated part of Onnertz' work, and found that his white crystalline product melted at 117–18° and was not 3-aminophthalic acid, but an acid ammonium salt of that compound.

Finally, Kahn,[16] in the course of the same year, reduced the nitro acid with hydrogen sulphide, observing, somewhat indefinitely, that 3-aminophthalic acid was very unstable, and that it "disappeared when its aqueous solution was boiled."

Concerning derivatives of 3-aminophthalic acid, except in a

very few instances there is much of the same uncertainty as in the case of the free acid. Baeyer,[3] in 1877, by reducing the diethyl ester of 3-nitrophthalic acid, had prepared an oily product which, after standing, solidified and could be recrystallized from alcohol; this he considered diethyl 3-aminophthalate. Miller, however, in repeating the work four years later, obtained a yellow, odorless oil which merely darkened upon standing, and which could not be distilled without decomposition.

In addition to Miller's "tin double salt" alluded to in the foregoing pages—a substance for which the formula $C_6H_3(NH_2HCl)(COOH)_2 + SnCl_4 + 2H_2O$ was suggested by the discoverer, on the strength of a chlorine determination—a similar compound was obtained by Bernthsen and Semper,[7] in 1886, by the reduction of 3-nitrophthalic acid with zinc and acetic acid. The reaction product was a white crystalline mass, apparently of the composition $C_6H_3.NH_2(COOH)COO.Zn.COOCH_3$, and easily losing carbon dioxide.

Onnertz,[12] in connection with his work above-mentioned, prepared the silver and the copper salt of what he believed to be 3-aminophthalic acid. His analytical figures are fairly good.

Reference has already been made to the acid ammonium salt which Kauffmann and Beisswenger[15] identified in repeating Onnertz' work. This compound, they found, gave up ammonia upon melting, at 117–18°, thus, as well as by remaining for some time in aqueous solution, forming a yellow compound which did not melt at 280°. Reasoning from the fact that the latter gave 3-aminophthalimide when treated with ammonia, these investigators were led to believe that it might be 3-aminophthalic anhydride. At this time, Kauffmann and Beisswenger also prepared the above imide, melting at 256–7°, both by reducing 3-nitrophthalimide with zinc and hydrochloric acid and by treating 3-nitrophthalic acid with ammonium sulphide. The following year (1904), they continued the work,[17] obtaining 3-aminophthanil, melting at

180–6°, by a reduction of the corresponding nitro compound, as well as its acetyl derivative, melting at 191°.

Meanwhile, other experimenters were at work on similar lines. By treating Bernthsen and Semper's zinc acetate double salt with acetic anhydride, Kahn,[16] in 1903, prepared 3-acetylaminophthalic anhydride, melting at 181°. From this he sought to form the free anhydride, by hydrolysis with caustic alkali, but obtained only an impure product hardly worth analyzing.

A 3-aminophthalhydrazide also was prepared, in 1902, by Schmitz,[14] from hemimellitic acid urethane. This compound is described as melting above 300°.

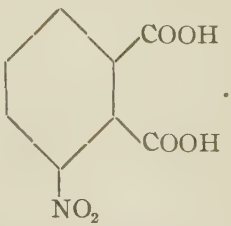
Finally, a 3-phenylglycinephthalic[9] acid, as well as a large number of dyes derived from 3-diazophthalic acid,[8] have been patented by Baeyer & Co., in 1889 and 1890.

In the course of the present study, most of the above work has been investigated. In general, the actual results given have been verified, but the conclusions in many cases have been found untenable. These will be discussed in the following pages, in their proper connection.

Experimental Part.

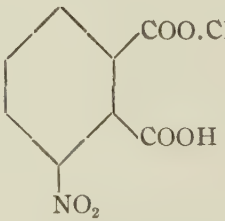
PREPARATION OF MOTHER-SUBSTANCES.

3-Nitrophthalic Acid,



. — This substance, which was used as a starting-point for all of the syntheses described further on, was prepared according to the method of Bogert and Boroschek,[11,4] by the nitration of phthalic anhydride, as follows:

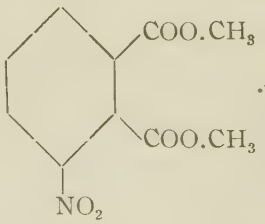
A mixture of 200 grams of phthalic anhydride, 200 cc. of fuming nitric acid and 160 cc. of concentrated sulphuric acid was heated in a porcelain casserole on the steam-bath, until the reaction began to take place with evolution of nitrous fumes. The casserole was then immediately removed and set aside until the reaction had subsided, after which it was again heated for two hours, with occasional stirring. After cooling, the solid mass consisting of 3-nitro- and 4-nitrophthalic acids was poured into 500 cc. of water, crushed with a pestle, and allowed to stand over night in the cold. It was then filtered out on cloth with suction, and washed with a little ice-water, after which the two nitrophthalic acids were separated by fractional crystallization. The mixture was dissolved in boiling water, evaporated until a thin crystalline film appeared on top of the solution, and then left undisturbed for five or six hours. The mother-liquor was poured off and evaporated for another crop, while the hard, yellowish crystals of 3-nitrophthalic acid deposited from both crystallizations were ground in a mortar, washed with a little ice-water, and recrystallized twice. The product so obtained consisted of pure white, prismatic needles melting at 221–2° (corr.) in a sealed tube; yield, 50 to 60 grams. 3-Nitrophthalic acid is described in the literature as a light yellow crystalline compound, but it is probable that the color is due to traces of picric acid which can be removed as shown above.

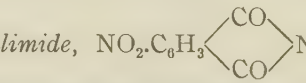
1-Methyl 3-Nitrophthalate, 

.—This compound was prepared according to Wegscheider's method,[19] as follows: 30 grams of nitrophthalic acid were placed in a flask together with 75 cc. of methyl alcohol and 6 grams of

concentrated sulphuric acid, and boiled under a reflux condenser for about eight hours. The solution was then diluted with cold water, and shaken in order that the ester might be deposited in crystalline form. When the latter had separated out completely, it was filtered out and washed with water. After dissolving in sodium carbonate solution, filtering from traces of neutral ester, and reprecipitating with dilute sulphuric acid, it was finally recrystallized from benzene, in white needles melted at 155–60°.

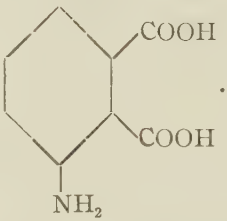
In the preparation of this compound, dry hydrochloric acid was used once or twice in place of sulphuric, as a condensing-agent, but without noticeable advantage. In both cases the yield was satisfactory.

Dimethyl 3-Nitrophthalate,  .—In order to esterify both carboxyls of 3-nitrophthalic acid, one molecule of the sodium salt was heated with two molecules of dimethyl sulphate in a porcelain casserole for about half an hour, with occasional stirring—or until the yellow organic salt was converted into white sodium sulphate. The mixture was then extracted with alcohol, from which the ester crystallized out in beautiful white prismatic needles, in almost quantitative yield. These were washed with water, in order to remove any trace of sodium sulphate, and when recrystallized a few times from alcohol melted at 68–9° (corr.).

3-Nitrophthalimide,  .—The method given by Bogert and Boroschek[11] was used in obtaining this substance: One molecule of 3-nitrophthalic acid was dissolved in a slight excess of ammonia, and the excess was expelled by

boiling. Another molecule of the acid was then added to the mixture and the whole evaporated to dryness and heated at 200° until no more moisture was given off. The dry mass was crystallized from alcohol-acetone, giving white crystals of 3-nitrophthalimide melting at 217–8° (corr.), in practically the theoretical amount.

3-AMINOPHTHALIC ACID AND DERIVATIVES.

3-Aminophthalic Acid, 

. — In attempting to prepare this rather elusive compound, five methods were used as follows, only the last two of which proved successful. It will be readily seen, from the properties of the acid, why the first three methods were unsatisfactory:

(*a*) *Reduction of 3-nitrophthalic acid with ammonium sulphide.*—Ten grams of the nitro acid were dissolved in enough sodium hydroxide solution to make the solution just alkaline, then ammonia was added, the solution warmed, and hydrogen sulphide passed into it for three and a half hours. The reason for first making a sodium salt of the nitro acid was to avoid the formation of an acid ammonium salt of the amino acid, which, according to the literature, cannot be readily decomposed into the free acid; while the ammonia was then used, instead of an excess of sodium hydroxide, for fear that long treatment with caustic alkali might destroy the unstable amino acid. After treatment with hydrogen sulphide, the solution was slightly acidified with hydrochloric acid and boiled for a while, in order to coagulate the sulphur liberated which was then filtered out. Upon partial evaporation a brownish-yellow crystalline deposit appeared on the sides of the vessel. This was washed with carbon disulphide, in order to remove

any sulphur present, and recrystallized from water. As a further means of purification the substance was dissolved in sodium carbonate solution and then acidified with acetic acid. As no precipitation occurred even on standing, the solution was extracted repeatedly with ether, and the extract evaporated. A yellowish residue was obtained, melting at about 160° both before and after recrystallization from water. Treatment with aniline, driving out excess, gave a substance melting at about 195°, which when acetylated melted at 213°. None of these melting-points agree with those of 3-aminophthalic acid, 3-aminophthalanil, or 3-acetylaminophthalanil as given elsewhere. It may be remarked that after reduction with hydrogen sulphide, all the solutions obtained in the above experiment were more or less fluorescent.

(*b*) *Saponification of the dimethyl ester of 3-aminophthalic acid with sodium ethylate.*—An alcoholic solution of the ester was boiled for about half an hour with sodium ethylate in slight excess of the theoretical amount. The granular precipitate formed was filtered out, washed with absolute alcohol and dissolved in water. It was found impossible, however, to liberate the free amino acid with hydrochloric acid, for one of the carboxyl groups retains its potassium with great tenacity, as will be shown in connection with the chemical properties of 3-aminophthalic acid.

(*c*) *Hydrolysis of 3-aminophthalimide with caustic alkali.*—As this method gave the anhydride and not the acid, it will be described elsewhere. Although potassium hydroxide was used in various dilutions, *viz.*, 5 per cent., 10 per cent. and 50 per cent., and the mixtures were heated for different lengths of time, it was found impossible to obtain the acid in this way.

(*d*) *Reduction of 3-nitrophthalic acid with tin and hydrochloric acid.*—Twenty grams of the nitro acid were placed in a beaker with 500 cc. of concentrated hydrochloric acid. This mixture was cooled to 5° and kept at that temperature, and while it was stirred by means of a turbine, granulated tin was added in small quantities from time to time, for about nine

hours. (It was found necessary, in repetitions of this process, to first crush the nitro acid to a very fine powder, for, otherwise, it did not reduce readily nor completely, and often gave an impure product.) By this time, grayish-white needles began to precipitate, and the mixture was left over night in the ice-chest in order to complete the precipitation. The needles, which appear by their chlorine content to be the hydrochloride of the amino acid, were then filtered on cloth, dissolved in moderate excess of cold water, filtered from residual impurities, reprecipitated with hydrochloric acid gas, and after several times repeating this process of purification, were finally dried in a vacuum desiccator over sulphuric acid and caustic soda, the removal of any free hydrochloric acid being found essential for the precipitation of the free acid. The yield of hydrochloride was satisfactory. The cake of dried needles was then pulverized, and dissolved in water as follows: About 25 cc. of water were placed in a beaker, and the hydrochloride was added in small portions, each portion being dissolved by agitating the beaker before more was added, until the solution became slightly turbid. Hereupon it was immediately filtered with suction, and the process was repeated with fresh water and hydrochloride, as many times as required. These precautions were necessary for several reasons: first, the aqueous solution of the hydrochloride is apt to contain dust and small particles of undissolved hydrochloride, which must be removed by filtration; secondly, the solution must be concentrated, in order to deposit the free acid; thirdly, the mechanical scratching of the hydrochloride particles against the sides of the beaker for too long a time or in large quantities causes the amino acid to separate out before the last traces of hydrochloride have dissolved. The vessel containing the combined filtrates was placed in the ice-chest for about an hour, with occasional stirring and scratching of the sides of the vessel, until the precipitation was complete. The white crystalline product so obtained was filtered, washed with a little ice-water, and dried in a desiccator. It was found to be 3-aminophthalic acid. The yield of free acid was about 25 per cent. of the hydro-

chloride used, but most of the hydrochloride could be recovered by saturating the mother-liquor with dry hydrochloric acid.

(*e*) *Reduction of 3-nitrophthalic acid with stannous chloride.* —This method, while based on practically the same reactions as the preceding, is preferable, inasmuch as it is more rapid and requires less attention. 10 grams of finely powered nitrophthalic acid were placed in a beaker, together with 50 grams of stannous chloride and 300 cc. of concentrated hydrochloric acid, and the whole stirred mechanically, at room temperature, for two or three hours, until the solution was complete, very little heat being developed during the reaction. In case a few granules of nitro acid remained, these were separated by decantation, or else the solution was warmed to 70 or 80°, and the stirring was continued until the fine white needles of hydrochloride began to separate. The mixture was chilled, and the needles filtered out and purified as already indicated. They were thus prepared as pure white without any grayish tinge. The rest of the procedure was identical with that described in the foregoing method.

3-Aminophthalic acid, as obtained by the above methods, is a white crystalline compound melting at 177° (corr.) when heated rapidly. At this temperature it effervesces and immediately resolidifies on the sides of the capillary, melting again at 185-6° (corr.), though not very sharply (cf. melting-point of 3-aminophthalic anhydride). When heated slowly, the acid begins to soften at 177° (corr.) and gradually decomposes until it melts completely at 191° (corr.). It is insoluble in benzene, chloroform and ligroïn; not very soluble in cold water; soluble in ether, ethyl (95 per cent. and absolute) and methyl alcohols, from which, however, it cannot be crystallized except by total evaporation attended with discoloration. Boiling with alcohol causes partial decomposition and marked fluorescence, while boiling with water gives a fluorescent solution which, on standing, deposits orange-yellow crystals melting with decomposition at 240° (corr.) on rapid heating. When heated with concentrated hydrochloric acid, 3-aminophthalic acid forms the hydro-

chloride, which crystallizes on cooling; the same hydrochloride is obtained in an amorphous condition when a fresh alcoholic solution of the amino acid is saturated with dry hydrochloric acid. Acetic anhydride acts upon the acid, giving 3-acetylaminophthalic anhydride, while aniline combines with it to form 3-aminophthalanil—all of which derivatives are described elsewhere. It decomposes sodium carbonate solution readily, and dissolves in caustic alkali.

The behavior of alkaline solutions of 3-aminophthalic acid toward acids is worthy of note for its peculiarity—concentration and length of time taken in neutralizing being, apparently, determining factors as to the nature of the compound formed. If the acid be dissolved in 10 per cent. potassium hydroxide, and the equivalent amount of 10 per cent. hydrochloric acid be added rapidly, the amino acid is reprecipitated after standing a few minutes. If, on the other hand, the neutralization be carried on slowly, or if stronger alkali and hydrochloric (or acetic) acid be used, the acid potassium salt crystallizes out in place of the free acid. Further acidification fails to decompose this acid salt; it dissolves in excess of hydrochloric acid, it is true, but once formed, it seems to exclude the precipitation of any free amino acid. When an ammoniacal solution of the acid is similarly treated, a corresponding acid ammonium salt is obtained, possessing like properties. This is evidently one of the compounds that balked the efforts of previous investigators to prepare the free acid. In order to see, furthermore, whether 3-aminophthalic anhydride could possibly be formed from the acid as it is from the imide, the neutral potassium salt being theoretically the intermediate product in both cases, the acid was boiled for a few moments with 10 per cent. caustic alkali and neutralized, while still warm, with the equivalent hydrochloric acid. The anhydride was not formed, however, but again the free acid. It is rather remarkable, in this connection, that the amino acid, which is so sensitive toward neutral solvents such as water and alcohol, will stand boiling with alkali.

Upon analysis of 3-aminophthalic acid the following figures were obtained:

0.2 gram gave 13.7 cc. N at 17° and 765 mm.
Found: N, 8.0 per cent. Calculated for $C_8H_7O_4N$: N, 7.7 per cent.
0.2 gram gave 0.3902 gram CO_2 and 0.0712 gram H_2O.
Found: C, 53.2 per cent.; H, 3.9 per cent.
Calculated for $C_8H_7O_4N$: C, 53.0 per cent.; H, 3.9 per cent.

It should be added, that neither 3-aminophthalic acid nor any of its derivatives gave the isonitrile test except after fusion with caustic alkali.

The compound mentioned above as melting at 240° was met with on other occasions, as will be shown in the following pages. When analyzed by the Dumas method, after drying at 110°,

0.2 gram gave 16.2 cc N at 19° and 758 mm.
Found: N, 9.2 per cent.

Judging from these figures, it is possible that the compound is a polymolecular imide, the theoretical nitrogen content being 9.6 per cent. in the case of a closed chain, and somewhat less for an open chain. The compound, however, was not studied in detail.

Hydrochloride of 3-Aminophthalic Acid, $HCl.NH_2.C_6H_3.(COOH)_2$.—This compound, which has been alluded to before, was obtained in four ways, *viz.*, by the reduction of 3-nitrophthalic acid, either with tin and hydrochloric acid or with stannous chloride, and by recrystallizing either 3-aminophthalic acid or its anhydride from strong hydrochloric acid. The details of these methods are given in connection with the notes on 3-aminophthalic acid and 3-aminophthalic anhydride respectively.

The hydrochloride consists of fluffy white needles melting with decomposition at 227° (corr.) when heated rapidly; gradual heating causes them to decompose slowly from 210° to 278°, at which temperature they melt. It is extremely soluble in water, in which it dissociates, precipitating the free amino acid when the solution is sufficiently concentrated. When boiled

with aniline it gives 3-aminophthalanil; with acetic anhydride 3-acetylaminophthalic anhydride. On ignition the hydrochloride leaves no ash.

In order to ascertain the cause of the discrepancy between the above results and those obtained by Miller,[6] who claimed that the "tin double salt" of 3-aminophthalic acid underwent a loss of carbon dioxide during the process of de-tinning, leaving *m*-aminobenzoic acid, the following tests were made.

3-Aminophthalic acid was reduced with tin and hydrochloric acid, as previously. The crude product of white needles obtained melted indefinitely above 200° and left some ash on ignition, as might be expected, but after twice dissolving in water and reprecipitating with gaseous hydrochloric acid, or likewise after twice dissolving in boiling concentrated hydrochloric acid and allowing to crystallize, these needles melted more sharply at 227° (corr.), and gave no ash. A small portion of each sample thus purified was treated with water, and 3-aminophthalic acid was obtained from both, melting at 177° (corr.) The hydrochloride was then dissolved in sufficient water to prevent the precipitation of the free acid, and the solution saturated with hydrogen sulphide. An insignificant amount of yellowish precipitate appeared (probably sulphur), after removing which, the solution was saturated a second time without further effect. Dry hydrochloric acid was then passed into the solution, as above, and upon cooling, the hydrochloride of 3-aminophthalic acid again crystallized out, melting at 227° (corr.) as before, and again forming 3-aminophthalic acid, melting at 177° (corr.), when hydrolyzed with a small quantity of water. The hydrochloride was next dissolved in hot hydrochloric acid, sp. gr. 1.1, and boiled for a few minutes. Upon cooling, the same compound no longer recrystallized, but instead there was obtained a good yield of stiff white needles melting with decomposition at 295° (corr.), which, when dissolved in a few drops of ammonia and neutralized with glacial acetic acid, gave a white crystalline precipitate melting at 174°. The latter compound was found to be identical with *m*-aminobenzoic acid (Kahlbaum), by taking

the melting-point of mixtures of the two, while the stiff needles corresponded exactly with the compound obtained by recrystallizing the Kahlbaum product from hydrochloric acid.

It is evident, therefore, that neither hydrogen sulphide nor boiling *concentrated* hydrochloric acid has any markedly destructive effect on the molecule of 3-aminophthalic acid hydrochloride. This compound is, however, sensitive to *dilute* hydrochloric acid, boiling with which causes it to split off carbon dioxide. It will be seen that the latter property is common also to the methyl esters of 3-aminophthalic acid.

With reference to the "tin double salt" of Miller, it must be added that this compound was not met with in any of the above experiments, unless the crude product obtained immediately after reduction, justify such a description. To all appearances however, this substance was identical with the hydrochloride obtained later, except in point of purity. In order to test whether concentration had any effect upon the formation of a tin double salt, the reduction was carried out at 60° with only 100 cc. of hydrochloric acid instead of 300, but in this case, even though the whole mixture solidified upon cooling, the reaction-product was in no respect different from that obtained by the usual method.

Acid Potassium Salt of 3-Aminophthalic Acid, $NH_2.C_6H_3.(COOH)COOK$.—This was formed when 3-aminophthalic acid was dissolved in potassium hydroxide solution and neutralized slowly with hydrochloric or acetic acid. It was precipitated as a white curdy mass which decomposed without melting at about 300°. It is fairly soluble in water, but does not give the free acid when acidified. It decomposes sodium carbonate.

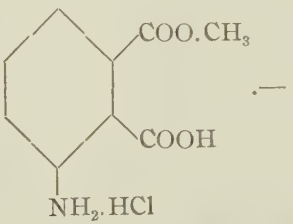
Acid Ammonium Salt of 3-Aminophthalic Acid, $NH_2.C_6H_3.(COOH)COONH_4$.—This compound was precipitated in the same way as the corresponding potassium salt, by the gradual neutralization of ammoniacal 3-aminophthalic acid. It occurs in microscopic white needles melting at 116-18° (corr.) with evolution of gas. Kauffmann and Beisswenger[15] claimed that the compound gives off ammonia at this temperature, giving a

compound with high melting-point—possibly 3-aminophthalic anhydride. This was not found to be the case, however. The ammonia could not be detected, neither was the anhydride identified as one of the products of decomposition. After melting at the above temperature, the compound solidified and remelted with effervescence at about 179°, then resolidified, turning red and decomposing finally at about 320°. The acid ammonium salt gives off ammonia when treated with caustic alkali solution, but does not give the free acid when acidified.

Silver 3-Aminophthalate, $NH_2.C_6H_3(COOAg)_2$.—This salt was formed by dissolving the acid in a slight excess of ammonia, adding a solution of silver nitrate, and neutralizing with dilute nitric acid, drop by drop, until the precipitation was complete. The salt was thus thrown out in very fine white crystalline flakes which had a silvery lustre when dried. Although it is stable in the ordinary atmosphere, it darkens considerably upon recrystallization from water—in which it is but slightly soluble. When heated to about 200°, the salt decomposes without melting.

Barium 3-Aminophthalate, $NH_2.C_6H_3(COO)_2Ba$.—When barium chloride solution was added to an ammoniacal solution of 3-aminophthalic acid, the barium salt was formed as a heavy, white precipitate. It is very sparingly soluble in cold, and not much more so in boiling water. By dissolving in the latter and evaporating down, it can be obtained in a somewhat granular condition.

Hydrochloride of 1-Methyl 3-Aminophthalate,



As 3-aminophthalic acid, upon acetylation, gave a symmetrical acetylamino anhydride and not an acetylanthranil, it was sought

to obtain a compound of the latter type by first "muzzling" the outer carboxyl, thus involving the amino group in the subsequent elimination of water. 1-Methyl 3-nitrophthalate was therefore used as a starting-product. 10 grams of the ester were finely pulverized and reduced with 50 grams of stannous chloride and 200 cc. of concentrated hydrochloric acid, the mixture being stirred by means of a water-motor. When a clear solution was thus formed, any remaining particles of the unreduced mother-substance were filtered out, and the stirring was continued until the hydrochloride of the amino ester began to separate in fine white needles. The precipitation was then completed by setting the vessel in the ice-chest. The needles were filtered on cloth and either recrystallized from concentrated hydrochloric acid or dissolved in water and salted out with hydrochloric acid gas. When purified two or three times in this manner, the compound was dried over sulphuric acid and caustic alkali in a vacuum desiccator, and was found to melt with evolution of gas at 153° (corr.) Upon analysis,

(I) 0.2 gram gave 10.6 cc. N at 24° and 752 mm.
Found: N, 5.8 per cent.
(II) 0.2 gram gave 10.8 cc. N at 21° and 751 mm.
Found: N, 6.0 per cent.
(III) 0.1 gram gave 5.3 cc. N at 21° and 767 mm.
Found: N, 6.09 per cent.
Calculated for $C_9H_{10}O_4NCl$. N, 6.04 per cent.

The hydrochloride is very soluble in water and in absolute alcohol. Like the hydrochloride of 3-aminophthalic acid, it breaks down into the hydrochloride of *m*-aminobenzoic acid when boiled with dilute hydrochloric acid. It was not found possible, however, to dissociate it into the free 1-methyl 3-aminophthalate by dissolving it in a small quantity of water as in the case of 3-aminophthalic acid. When recrystallized from this solvent, it deposited reddish crystals melting at 240°, obtained similarly from 3-aminophthalic acid or its anhydride. Upon acetylation of the hydrochloride, white needles were ob-

tained which melted at about 175°; these, however, when boiled with ammonia and a little caustic alkali, then acidified, did not give 2-methyl 4-ketodihydroquinazoline-5-carboxylic acid which might have been expected had the acetylated product been the acetylanthranil.

1-Methyl 3-nitrophthalate was reduced a number of times as above described, with uniform results. In one instance, however, needles melting at about 280° instead of at 153° were obtained. These were boiled with acetic anhydride, giving white crystals melting at about 180°, which, in turn, when boiled with ammonia and dilute caustic alkali, and acidified, gave a white crystalline compound melting with decomposition at the same temperature as the quinazoline referred to. This isolated case, however, is hardly conclusive of the formation of an acetylanthranil, especially as the experiment was made on rather small amounts, and not enough of the reaction-products was obtained for purification and analysis.

Dimethyl 3-Aminophthalate, $NH_2.C_6H_3(COOCH_3)_2$.—The method used in the preparation of this compound was practically the same as that used by Baeyer,[3] and by Bogert and Renshaw,[18] in obtaining the corresponding ester of 4-aminophthalic acid. 25 grams of the dimethyl ester of 3-nitrophthalic acid were dissolved in alcohol and added to 250 cc. of concentrated hydrochloric acid, which caused the ester to reprecipitate in finely divided form. The mixture was cooled to 0° and maintained at that temperature, while granulated zinc was added in small quantities from time to time, the liquid being stirred with a turbine. In about three hours, when the solution was perfectly clear, it was nearly neutralized with sodium hydroxide, and sodium carbonate was added until the precipitate formed redissolved with difficulty. An excess of sodium acetate was then added, and a little reddish-brown oil separated out. The whole mixture was then repeatedly extracted with ether, and upon evaporation of this solvent, about 19 grams of the oil were obtained. This oil had a pleasant odor suggesting that of Concord

grapes, but smelled strongly of acetic acid. This objection was obviated by omitting the use of sodium acetate.

In order to purify the oil, it was distilled under diminished pressure, but without success, for the substance decomposed considerably even when the pressure was reduced to from 9 to 12 mm. its boiling-point under those conditions being above 170°. Crystallization from water, alcohol, chloroform, benzene and benzene-ligroïn was then tried with no better results. Finally, after long standing over sulphuric acid in a vacuum desiccator, some of the oil solidified in a dark brown, waxy mass with low, but indefinite, melting-point.

The oil readily formed an acetyl derivative which proved to be the dimethyl ester of 3-acetylaminophthalic acid. It also dissolved quite readily in hydrochloric acid. All neutral solutions of this oil were highly fluorescent, even when extremely dilute.

As the crude product thus obtained did not admit of purification, an attempt was made to prepare the ester in a manner similar to that used in the formation of the free acid. 5 grams of the nitro ester were placed in a beaker with 100 cc. of concentrated hydrochloric acid, and granulated tin was added from time to time until all of the ester had gone into the solution. The liquid was then chilled, but even after standing over night in the cold, no crystallization took place. After resaturating the solution with gaseous hydrochloric acid without effect, the mixture was evaporated to one-half its volume, diluted with 300-400 cc. of water, and de-tinned with hydrogen sulphide. The clear solution was then concentrated, but upon cooling, deposited the hydrochloride of *m*-aminobenzoic acid, m. 295° (corr.), and not that of the aminophthalic ester.

The failure to obtain the latter compound by salting out with hydrochloric acid, was probably due to its extreme solubility in that reagent, as will be shown later. It is reasonable to suppose that the hydrochloride of the ester does exist in the solution and that boiling down with dilute acid causes, first, a saponification, and then a loss of carbon dioxide in accordance with the reac-

tions described above in the case of the hydrochloride of 3-aminophthalic acid.

Hydrochloride of Dimethyl 3-Aminophthalate, $HCl.NH_2.C_6H_3.(COOCH_3)_2$.—This was prepared by passing dry hydrochloric acid into a benzene solution of the free ester, out of which it formed as a light pink precipitate, somewhat gelatinous when in suspension. The compound was washed with benzene and dried in a vacuum desiccator. When dry it melted with decomposition at 172-4° (corr.), and was hygroscopic, becoming sticky when left in the open atmosphere. Upon treatment with a little water it dissociated, giving back the oily ester with its characteristic odor. It was found impossible to recrystallize the salt from hydrochloric acid either strong or dilute, owing to its extreme solubility in those solvents.

Dimethyl 3-Acetylaminophthalate, $CH_3CO.NH.C_6H_3(COOCH_3)_2$. —This derivative was obtained by boiling the oil considered above to be the dimethyl ester of 3-aminophthalic acid with an excess of acetic anhydride. The reaction-product was dissolved in boiling water, and whatever tarry residue was present, was filtered out. On cooling, the acetyl compound crystallized, although occasionally it came down as an oil, in which case seeding or scratching was resorted to. For further purification the compound was recrystallized from 1 per cent. aqueous acetic acid.

Dimethyl 3-acetylaminophthalate is dimorphic, forming both hard, white, rhombic crystals and fluffy plates melting at 92-3° (corr.), which exhibit strong tribo-luminescence, even under water. Its solutions in water, alcohol, chloroform, or acetic acid are somewhat fluorescent, but less so than those of the unacetylated oil. With aniline it combines, giving 3-acetylaminophthalanil, and with ammonia it condenses to form 2-methyl 4-ketodihydroquinazoline-5-carboxylic acid.

Analysis:

0.2 gram gave 10.1 cc. N at 23° and 758 mm.

Found: N, 5.57 per cent.

Calculated for $C_{12}H_{13}O_5N$: N, 5.67 per cent.

The ester seems to be unreactive toward bromine. Neither in glacial acetic acid nor in chloroform solution did any absorption of halogen take place, but in both cases the ester was recovered unaltered.

A condensation with phenylhydrazine was also tried, but the reaction-product was a tarry mass which could not be induced to crystallize from the common solvents.

3-Aminophthalic Anhydride, $NH_2.C_6H_3\begin{matrix}CO\\ \\ CO\end{matrix}O$.—When 3-aminophthalimide was treated with caustic alkali, the anhydride was formed, it has been remarked, and not the free acid. In this experiment, 1 gram of the imide was boiled for about half an hour with 10 cc. of standard 10 per cent. potassium hydroxide solution, replacing any water lost by evaporation. During the reaction ammonia was liberated, giving tests with moist litmus paper and by slight odor, and the object of continued boiling was to expel the ammonia. While still warm, the solution was neutralized very exactly with standard 10 per cent. hydrochloric acid, whereupon a lemon-yellow crystalline precipitate formed. After standing for some time in the cold, with occasional scratching of the beaker, this was filtered out, washed with a little cold water, dried over sulphuric acid and recrystallized from absolute alcohol. Light yellow needles were thus obtained, which melted at 193-4° (corr.), and gave the following figures on analysis:

> From 0.2 gram substance, 15.2 cc. of N at 24° and 769 mm.
> Found: N, 8.62 per cent.
> Calculated for $C_8H_5O_3N$: N, 8.59 per cent.

That the compound was the symmetrical anhydride and not the corresponding anthranil, was indicated by the reaction of its acetyl derivative with aniline, forming 3-acetylaminophthalanil instead of a quinazoline.

3-Aminophthalic anhydride is soluble in alcohol, acetone, chloroform and ether with strong fluorescence; insoluble in benzene and ligroïn. From aqueous alcohol (95 per cent.) it may

be recrystallized with considerable loss, and even when anhydrous alcohol is used, the yield is only about $^2/_3$ of the amount dissolved, the loss being due possibly to the formation of oily esters. Chloroform-ligroïn is perhaps the best medium for recrystallization. When dissolved in boiling water the anhydride deposits orange-yellow crystals melting at 240° (corr.), identical with those obtained from 3-aminophthalic acid under similar conditions. In order to obtain a hydrochloride, an acetone solution of the anhydride was saturated with dry hydrochloric acid, but without success. An anhydrous alcoholic solution, when similarly treated, gave nothing but a sticky residue; however, when the anhydride was dissolved in hot concentrated aqueous hydrochloric acid, the hydrochloride of 3-aminophthalic acid was produced. On acetylation the amino anhydride gave the acetylamino anhydride, described below.

3-Acetylaminophthalic Anhydride, $CH_3CO.NH.C_6H_3\begin{matrix}CO\\ \diagup\diagdown O\\ CO\end{matrix}$. —This compound, already prepared by Kahn,[16] was obtained by acetylating either 3-aminophthalic acid or its hydrochloride, or 3-aminophthalic anhydride. The respective substances were boiled with acetic anhydride, and upon cooling, the compound crystallized out in cream-white needles which were afterward recrystallized from alcohol.

3-Acetylaminophthalic anhydride melts at 185-6° (corr.). When heated with aniline it forms 3-acetylaminophthalanil. On analysis,

0.2 gram gave 12.2 cc. of N at 22° and 758 mm.
Found: N, 6.89 per cent.
Calculated for $C_{10}H_7O_4N$: N, 6.82 per cent.

3-Aminophthalimide, $NH_2.C_6H_3\begin{matrix}CO\\ \diagup\diagdown NH\\ CO\end{matrix}$. — According to Kauffmann and Beisswenger,[15] the best method for preparing this compound is to reduce the free nitro acid with ammonium sulphide and then to heat the acid ammonium salt formed, with elimination of one molecule of water. In the present work,

three methods were used, the first of which was a modification of Kauffmann and Beisswenger's, the condensation of the imide ring being carried out before instead of after the reduction:

(*a*) *Reduction of 3-nitrophthalimide with ammonium sulphide.*—10 grams of the nitro imide were warmed with an excess of ammonia water and a few cubic centimeters of alcohol, and the mixture was saturated with hydrogen sulphide for about three hours. At the end of this time the dark red solution was allowed to cool, and deposited the amino imide in fine yellowish needles. These were recrystallized from acetone, and were found to melt at about 255-8°, with darkening, probably due to a trace of sulphur. The yield was about 4 grams.

(*b*) *Reduction of 3-nitrophthalimide with zinc and hydrochloric acid.*—This process was carried out just as in the preparation of dimethyl 3-aminophthalate. It was unsatisfactory, however, the yield of amino imide being very small.

(*c*) *Reduction of 3-nitrophthalimide with stannous chloride.*—This method was by far the best, the yield being practically quantitative, and the amino imide thus obtained melting without discoloration. 30 grams of the nitro imide were stirred mechanically with about 120 grams of stannous chloride and 500 cc. of concentrated hydrochloric acid, until the imide went into solution with liberation of heat. Upon cooling, the hydrochloride of the amino imide appeared as a cream-white precipitate. This was filtered out, and converted into the free imide by contact with water, with which it was carefully washed. Crystallization from alcohol gave over 25 grams of bright yellow needles melting at 266–7° (corr.).

Analysis:

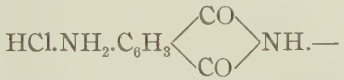
0.1 gram gave 15.4 cc. N at 21° and 759 mm.
Found: N, 17.5 per cent.
Calculated for $C_8H_6O_2N_2$: N, 17.3 per cent.

3-Aminophthalimide is moderately soluble in the common organic solvents. In alcohol or acetone it shows an intense green-yellow fluorescence, while its solution in chloroform or

ether is colorless, with blue-violet fluorescence. This property of fluorescence is possessed even by the dry yellow needles, which have an indefinite tinge of green about them. The compound may be crystallized in long needles out of a large bulk of water. It is soluble also in concentrated hydrochloric acid, but recrystallizes from that solvent as a hydrochloride. Upon treatment with aqueous caustic alkali it loses ammonia, giving 3-aminophthalic anhydride when neutralized, while alcoholic potash converts it into the potassium imide. The imide also acetylates quite readily.

As a condensation between 3-aminophthalimide and cyanic acid showed interesting possibilities, several attempts were made to bring this about. The imide was dissolved in acetone, a little aqueous potassium cyanate was added, and after cooling the mixture to 0°, the calculated amount of concentrated hydrochloric acid was introduced drop by drop, with stirring. Nothing else was obtained, however, than the hydrochloric salt of the imide, which was precipitated. Some of this hydrochloride was then ground in a mortar with dry cyanate, but although the moisture in the air caused the hydrochloride to dissociate, the free imide thus formed was left unchanged. Again, equivalent amounts of hydrochloride and cyanate were placed together in a stoppered flask, in acetone suspension. After standing for over two weeks, however, no reaction seemed to have taken place. Water was then added gradually, and the hydrochloride was decomposed into the free imide. Finally, some imide was placed in dilute hydrochloric acid, and to the ice-cold mixture, cyanate solution was added slowly; the suspended imide was unaffected, just as in the previous instances.

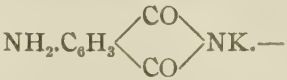
Hydrochloride of 3-Aminophthalimide,



This was obtained as a white granular precipitate, in the reduction of 3-nitrophthalimide with stannous chloride. It melts with decomposition at 268° (corr.) when heated rapidly, and is immediately dissociated into the free imide in the presence of

water. The hydrochloride may also be formed by crystallizing 3-aminophthalimide from concentrated hydrochloric acid, and may be precipitated with dry hydrochloric acid from an acetone solution of the imide.

Potassium Salt of 3-Aminophthalimide,



When a solution of 3-aminophthalimide in absolute alcohol was boiled with anhydrous alcoholic potash, a cream-white precipitate was formed, which was believed to be its potassium salt. This was thoroughly washed with absolute alcohol and dried in a vacuum desiccator. When treated with water, this compound immediately gave back the free imide, and even on standing in a stoppered vessel, was slowly hydrolyzed by the moisture of the air.

In order to prepare 3-aminophthalmethylimide, this potassium salt was treated with dimethyl sulphate. A vigorous reaction took place, with development of heat, and upon neutralization with sodium carbonate a yellow compound was precipitated which recrystallized from alcohol in fine needles melting at about 145°. Analysis indicated this substance to be 3-dimethylaminophthalmethylimide, however, and not 3-aminophthalmethylimide. In this reaction other compounds were also formed in small amounts, but were not further investigated.

3-Acetylaminophthalimide, —This compound was obtained by the acetylation of 3-aminophthalimide. The imide was boiled for a few moments with just enough acetic anhydride to dissolve it, and the acetylated product was allowed to crystallize out. Ethyl acetate was found to be most satisfactory for subsequent recrystallizations.

3-Acetylaminophthalimide, when pure, melts at 242° (corr.). It is moderately soluble in alcohol and ethyl acetate, from which it crystallizes in white granular crystals, and is still

less soluble in boiling water, out of which it may be obtained in needles. When heated with dilute caustic alkali, it readily condenses into 2-methyl-4-ketodihydroquinazoline-5-carboxylic acid.

Analysis:

0.1 gram gave 12.3 cc. N at 20° and 754 mm.
Found: N, 13.9 per cent.
Calculated for $C_{10}H_8O_3N_2$: N, 13.7 per cent.

An attempt was made to brominate this compound. A small portion was dissolved in glacial acetic acid, and a slight excess of bromine was added. No discoloration was noticeable, however, even upon standing. When the bromine had been expelled by boiling, the original substance was recovered unchanged by simply diluting with water.

3-Diacetylaminophthalimide, $(CH_3CO)_2N.C_6H_3\begin{matrix}CO\\ \diagup\diagdown\\ CO\end{matrix}NH.$ —

Upon boiling 3-aminophthalimide for a little while with a considerable excess of acetic anhydride, and taking up the solution with absolute alcohol in order to decompose the excess of reagent, a diacetyl derivative was found to crystallize out, instead of the monoacetyl described above. This compound, when recrystallized two or three times from absolute alcohol, melted at 152–4° (corr.), and analyzed as follows:

0.1 gram gave 10.4 cc. N at 24° and 758 mm.
Found: N, 11.6 per cent.
Calculated for $C_{12}H_{10}O_4N_2$: N, 11.4 per cent.

When recrystallized from boiling water, the compound hydrolyzed partially, giving the monoacetyl derivative.

3-Phenyluraminophthalimide,

$$C_6H_5.NH.CO.NH.C_6H_3\begin{matrix}CO\\ \diagup\diagdown\\ CO\end{matrix}NH.—$$

When 3-aminophthalimide was boiled for a few moments with enough phenyl isocyanate to wet it thoroughly, the yellow

needles were converted into a white amorphous powder without first going into solution. This product was washed with absolute alcohol in order to free it from the excess of reagent and from diphenylurea, and was crystallized from 30–40 per cent. alcohol from which it was obtained in flocculent white needles which packed down tightly upon filtration. When heated they became amorphous at about 260° (corr.) and melted with darkening at about 335° (corr). Analysis showed the compound to be 3-phenyluraminophthalimide:

0.1 gram gave 13.4 cc. N at 19° and 753 mm.
Found: N, 15.2 per cent.
Calculated for $C_{15}H_{11}O_3N_3$: N, 14.9 per cent.

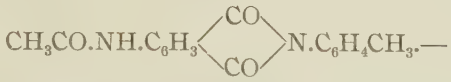
3-Aminophthalanil, $NH_2.C_6H_3\begin{matrix}CO\\ \diagup\\ \diagdown\\ CO\end{matrix}N.C_6H_5$. — This compound, already isolated by Kauffmann and Beisswenger,[17] was obtained in these experiments by heating 3-aminophthalic acid, or its anhydride, with aniline, boiling off the excess of solvent, and crystallizing from alcohol, out of which it formed in pale yellow needles melting at 186–8° (corr.). When it was prepared from 3-aminophthalimide, it was found rather difficult to remove traces of undecomposed imide, and therefore the first two methods mentioned are preferable.

3-Acetylaminophthalanil, $CH_3CO.NH.C_6H_3\begin{matrix}CO\\ \diagup\\ \diagdown\\ CO\end{matrix}N.C_6H_5$. —

As recorded by Kauffmann and Beisswenger,[17] this substance is readily formed by acetylating 3-aminophthalanil. In the course of the present investigations, it was prepared also by heating the dimethyl ester of 3-acetylaminophthalic acid with an excess of aniline, expelling the excess, and crystallizing from alcohol. The product so obtained consisted of needles melting at 195.5° (corr.), and was lighter in color than that obtained by the former method, being nearly cream-white. The analytical figures obtained gave the nitrogen content as 10.4 per cent. where the theoretical value is 10.0 per cent.

3-Acetylaminophthalanil was caused to condense with ammonia, giving a quinazoline which will be described further on.

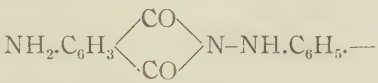
3-Acetylaminophthal-o-Tolil,



This compound was prepared analogously to the anil, by boiling dimethyl 3-acetylaminophthalate with *o*-toluidine. Several recrystallizations from methyl alcohol produced the compound in coarse straw-colored prisms melting at 214–5° (corr.). When the substance was dissolved in acetone and diluted with water, cream-white needles were precipitated, having the same melting-point. On analysis:

0.2 gram gave 17.2 cc. N at 21° and 759 mm.
Found: N, 9.7 per cent.
Calculated for $C_{17}H_{14}O_3N_2$: N, 9.5 per cent.

3-Aminophthalphenylhydrazide,



In order to prepare this substance, 3-aminophthalimide was heated in a beaker with enough phenylhydrazine to wet it thoroughly. After the imide had gone into solution the excess of phenylhydrazine was boiled off, and the red mass which solidified on cooling was recrystallized from 60 per cent. alcohol. The compound was thus obtained in deep yellow, crystalline flakes which melted with decomposition at 284–5° after softening somewhat below that temperature. Upon recrystallizing from the same solvent or from dilute acetone, the substance assumed a greenish tint, which deepened gradually to dark green during subsequent recrystallizations. The melting-point of the compound was not appreciably

affected, however. A Dumas combustion showed the following results:

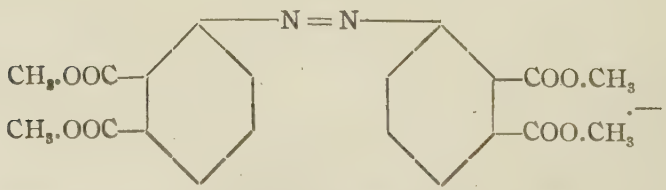
0.1 gram. gave 14.2 cc. N at 19° and 769 mm.
Found: N, 16.52 per cent.
Calculated for $C_{14}H_{11}O_2N_3$: N, 16.60 per cent.

In attempting to acetylate the phenylhydrazide, a small quantity was treated with acetic anhydride. A violent reaction took place, with immediate solidification, but the resulting mass could not be crystallized satisfactorily from any of the ordinary solvents. Another portion of the phenyl hydrazide was dissolved in glacial acetic acid and a slight excess of acetic anhydride was added. Yellowish needles were deposited on cooling, which, when recrystallized from alcohol, melted at 223–4° (corr.). Upon analysis:

0.1 gram gave 14.2 cc. N at 20° and 756 mm.
Found: N, 16.3 per cent.

The calculated figures for acetylaminophthalphenylhydrazide are: N, 14.2 per cent. The compound was set aside for later investigation.

Tetramethyl 3-Azophthalate,



In attempting to prepare dimethyl 3-aminophthalate, an alcoholic solution of the nitrophthalate was boiled with aluminium amalgam under a reflux condenser for several days. The red solution thus obtained, when filtered from the residue of amalgam and alumina, and concentrated, deposited orange-red needles melting at about 185°. Upon recrystallizing a number of times from alcohol, the melt-

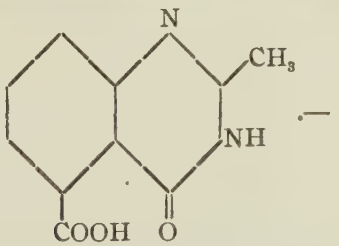
ing-point rose gradually to 224–5° (corr.), where it remained constant. Upon analysis:

0.1 gram gave 6.2 cc. N at 21° and 759 mm.
Found: N, 7.04 per cent.
Calculated for $C_{20}H_{18}O_8N_2$: N, 6.76 per cent.

The mother-liquors from the above recrystallizations were generally much lighter in color than the solutions of the orange needles, and deposited yellowish crystals which melted a little lower than the latter, although less sharply. On the ground that these might be the hydrazophthalate, they were treated with nitrous acid, which should have oxidized them to the azo condition, but without effect. They were not further investigated.

It may be added that the above reduction with aluminium amalgam was rather unsatisfactory, the method being slow and the yield poor.

2-Methyl 4-Ketodihydroquinazoline-5-carboxylic Acid,



In first preparing this quinazoline, 5 grams of dimethyl 3-acetylaminophthalate were heated for three hours at 150° in a sealed tube, with an excess of ammonia. The resulting solution was poured into a beaker and boiled with a little potassium hydroxide solution until the excess of ammonia was expelled. Enough dilute hydrochloric acid was then added to just pass the neutral point, when the quinazoline was precipitated in brownish needles. These were redissolved in boiling water, bone-blacked, and recrystallized until pure white. The experiment was repeated successfully, using

3-acetylaminophthalanil instead of the ester as a starting-point. Neither case, however, gave perfectly uniform results, for in repeating the work under apparently the same conditions, the quinazoline failed occasionally to appear, while there were obtained instead small quantities of products melting at about 320°, 197–9°, and 265?, which were not investigated.

A simpler and more satisfactory method was found, later, of isolating the quinazoline. 3-Acetylaminophthalimide was boiled with a slight excess of 5 per cent. caustic potash solution, then barely acidified with dilute hydrochloric acid. The quinazoline crystallized out in fairly pure form.

2-Methyl-4-ketodihydroquinazoline-5-carboxylic acid is rather insoluble in most solvents. It dissolves with difficulty in a large amount of boiling water, from which it crystallizes in clusters of white needles melting with decomposition at 342° (corr.) and crumbling to powder, even when allowed to stand for any length of time in the mother-liquor. It dissolves readily in alkali to form a salt, from which it can be reprecipitated by acidification. The following analytical data were obtained:

On heating at 110°, 0.2 gram lost 0.0246 gram, indicating $1\frac{1}{2}H_2O$ per molecule.

0.1754 gram (dried) gave 0.3974 gram CO_2 and 0.0640 gram H_2O.

Found: C, 58.9 per cent.; H, 4.0 per cent.

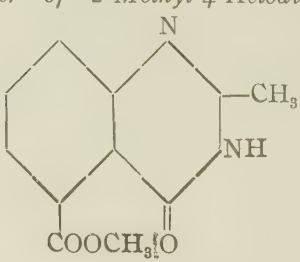
Calculated for $C_{10}H_8O_3N_2$: C, 58.8 per cent.; H, 3.9 per cent.

0.15 gram (dried) gave 18.6 cc. Nat 21° and 752 mm.

Found: N, 13.95 per cent.

Calculated for $C_{10}H_8O_3N_2$: N, 13.72 per cent.

Methyl Ester of 2-Methyl-4-Ketodihydroquinazoline-5-Carboxylic Acid,



.—The quinazoline

acid described in the preceding paragraph was esterified by treating its dry potassium salt with the calculated amount of dimethyl sulphate. The mixture was heated for a few moments with addition of a little potassium carbonate, and upon cooling, the ester separated out as a white precipitate. By recrystallizing from alcohol it was obtained in the form of soft white needles, very light and bulky, melting at 273–4° (corr.). Upon analysis:

0.1 gram gave 11.2 cc. N at 21° and 770 mm.
Found: N, 12.9 per cent.
Calculated for $C_{11}H_{10}O_3N_2$: N, 12.8 per cent.

Owing, however, to the small quantities of quinazoline acid available, difficulty was experienced in repeating the above esterification. Apparently, the reaction does not work well on the small scale.

Conclusions.

3-Aminophthalic acid can be prepared in the pure state by the reduction of 3-nitrophthalic acid with tin and hydrochloric acid or directly with stannous chloride.

The acid possesses properties similar to those of other aromatic dibasic amino acids. Thus, it forms an anhydride, various imides, and acid and neutral esters and salts, while its amino group reacts readily with acetic anhydride, phenyl isocyanate and mineral acids. In addition to this, the acid is capable of undergoing ortho condensations between the amino group and the adjacent carboxyl, forming quinazolines.

The acid and most of its simple derivatives are crystalline products, with definite melting-points and characteristic properties. They are stable at ordinary temperatures, but when heated, they for the most part either decompose or polymerize.

The acid itself is stable toward alkalies and toward concentrated mineral acid, but upon boiling with dilute mineral acid it readily loses carbon dioxide, leaving *m*-aminobenzoic acid. The latter property is common also to some of its derivatives.

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BIOGRAPHICAL NOTE.

The author of this dissertation was born in New York City, April 18, 1884. He entered Columbia University in the fall of 1900, receiving the degree of Bachelor of Arts from that institution in 1904. Since then he has been engaged in pursuing graduate work in chemistry and physics under the Faculty of Pure Science of Columbia University.

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A DISSERTATION

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